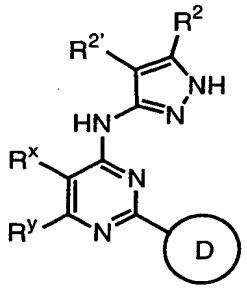
CLAIMS SET 3

We claim:

1. A compound of formula **IV**:



IV

or a pharmaceutically acceptable derivative or prodrug thereof, wherein:

Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl, said heteroaryl or heterocyclyl ring having 1-4 ring heteroatoms selected from nitrogen, oxygen or sulfur, wherein Ring D is independently substituted at any substitutable ring carbon by oxo or $-R^5$, and at any substitutable ring nitrogen by $-R^4$, provided that when Ring D is a six-membered aryl or heteroaryl ring, $-R^5$ is hydrogen at each ortho carbon position of Ring D;

R^x and R^y are independently selected from $T-R^3$, or R^x and R^y are taken together with their intervening atoms to form a fused, unsaturated or partially unsaturated, 5-8 membered ring having 1-3 ring heteroatoms selected from oxygen, sulfur, or nitrogen, wherein any substitutable carbon on said fused ring is optionally and independently substituted by $T-R^3$, and any substitutable nitrogen on said ring is substituted by R^4;

T is a valence bond or a C_{1-4} alkylidene chain;

R^2 and $R^{2'}$ are independently selected from -R, -T-W-R^6, or R^2 and $R^{2'}$ are taken together with their intervening atoms to form a fused, 5-8 membered, unsaturated or partially unsaturated, ring containing 0-3 ring heteroatoms selected from nitrogen, oxygen, or sulfur, wherein said fused ring is optionally substituted by up to three groups independently selected from halo, oxo, -CN, $-NO_2$, $-R^7$, or -V-R^6;

R^3 is selected from -R, -halo, =O, -OR, -C(=O)R, $-CO_2R$, -COCOR, $-COCH_2COR$, $-NO_2$, -CN, -S(O)R, $-S(O)_2R$, -SR, $-N(R^4)_2$, $-CON(R^4)_2$, $-SO_2N(R^4)_2$, -OC(=O)R, $-N(R^4)COR$, $-N(R^4)CO_2$(optionally substituted C_{1-6} aliphatic), $-N(R^4)N(R^4)_2$, $-C=NN(R^4)_2$, -C=N-OR, $-N(R^4)CON(R^4)_2$, $-N(R^4)SO_2N(R^4)_2$, $-N(R^4)SO_2R$, or $-OC(=O)N(R^4)_2$;

each R is independently selected from hydrogen or an optionally substituted group selected from C_{1-6} aliphatic, C_{6-10} aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 5-10 ring atoms;

each R^4 is independently selected from $-R^7$, $-COR^7$, $-CO_2$(optionally substituted C_{1-6} aliphatic), $-CON(R^7)_2$, or $-SO_2R^7$, or two R^4 on the same nitrogen are taken together to form a 5-8 membered heterocyclyl or heteroaryl ring;

each R^5 is independently selected from -R, halo, -OR, -C(=O)R, $-CO_2R$, -COCOR, $-NO_2$, -CN, -S(O)R, $-SO_2R$, -SR, $-N(R^4)_2$, $-CON(R^4)_2$, $-SO_2N(R^4)_2$, -OC(=O)R, $-N(R^4)COR$, $-N(R^4)CO_2$(optionally substituted C_{1-6} aliphatic), $-N(R^4)N(R^4)_2$, $-C=NN(R^4)_2$, -C=N-OR, $-N(R^4)CON(R^4)_2$, $-N(R^4)SO_2N(R^4)_2$, $-N(R^4)SO_2R$, or $-OC(=O)N(R^4)_2$;

V is -O-, -S-, -SO-, $-SO_2-$, $-N(R^6)SO_2-$, $-SO_2N(R^6)-$, $-N(R^6)-$, -CO-, $-CO_2-$, $-N(R^6)CO-$, $-N(R^6)C(O)O-$, $-N(R^6)CON(R^6)-$, $-N(R^6)SO_2N(R^6)-$, $-N(R^6)N(R^6)-$, $-C(O)N(R^6)-$, $-OC(O)N(R^6)-$, $-C(R^6)_2O-$, $-C(R^6)_2S-$,

$-C(R^6)_2SO-$, $-C(R^6)_2SO_2-$, $-C(R^6)_2SO_2N(R^6)-$, $-C(R^6)_2N(R^6)-$, $-C(R^6)_2N(R^6)C(O)-$, $-C(R^6)_2N(R^6)C(O)O-$, $-C(R^6)=NN(R^6)-$, $-C(R^6)=N-O-$, $-C(R^6)_2N(R^6)N(R^6)-$, $-C(R^6)_2N(R^6)SO_2N(R^6)-$, or $-C(R^6)_2N(R^6)CON(R^6)-$;

W is $-C(R^6)_2O-$, $-C(R^6)_2S-$, $-C(R^6)_2SO-$, $-C(R^6)_2SO_2-$, $-C(R^6)_2SO_2N(R^6)-$, $-C(R^6)_2N(R^6)-$, $-CO-$, $-CO_2-$, $-C(R^6)OC(O)-$, $-C(R^6)OC(O)N(R^6)-$, $-C(R^6)_2N(R^6)CO-$, $-C(R^6)_2N(R^6)C(O)O-$, $-C(R^6)=NN(R^6)-$, $-C(R^6)=N-O-$, $-C(R^6)_2N(R^6)N(R^6)-$, $-C(R^6)_2N(R^6)SO_2N(R^6)-$, $-C(R^6)_2N(R^6)CON(R^6)-$, or $-CON(R^6)-$;

each R^6 is independently selected from hydrogen or an optionally substituted C_{1-4} aliphatic group, or two R^6 groups on the same nitrogen atom are taken together with the nitrogen atom to form a 5-6 membered heterocyclyl or heteroaryl ring; and

each R^7 is independently selected from hydrogen or an optionally substituted C_{1-6} aliphatic group, or two R^7 on the same nitrogen are taken together with the nitrogen to form a 5-8 membered heterocyclyl ring or heteroaryl.

2. The compound according to claim 1, wherein said compound has one or more features selected from the group consisting of:

(a) Ring D is an optionally substituted ring selected from a phenyl, pyridinyl, piperidinyl, piperazinyl, pyrrolidinyl, thienyl, azepanyl, morpholinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, 2,3-dihydro-1*H*-isoindolyl, 2,3-dihydro-1*H*-indolyl, isoquinolinyl, quinolinyl, or naphthyl ring;

(b) R^x is hydrogen or C_{1-4} aliphatic and R^y is T-R^3, or R^x and R^y are taken together with their intervening atoms to form an optionally substituted 5-7 membered

unsaturated or partially unsaturated ring having 1-2 ring heteroatoms; and

(c) $R^{2'}$ is hydrogen or methyl and R^2 is T-W-R^6 or R, wherein W is $-C(R^6)_2O-$, $-C(R^6)_2N(R^6)-$, -CO-, $-CO_2-$, $-C(R^6)OC(O)-$, $-C(R^6)_2N(R^6)CO-$, $-C(R^6)_2N(R^6)C(O)O-$, or $-CON(R^6)-$, and R is an optionally substituted group selected from C_{1-6} aliphatic or phenyl, or R^2 and $R^{2'}$ are taken together with their intervening atoms to form a substituted or unsubstituted benzo, pyrido, pyrimido, or partially unsaturated 6-membered carbocyclo ring.

3. The compound according to claim 2, wherein:

(a) Ring D is an optionally substituted ring selected from a phenyl, pyridinyl, piperidinyl, piperazinyl, pyrrolidinyl, thienyl, azepanyl, morpholinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, 2,3-dihydro-1*H*-isoindolyl, 2,3-dihydro-1*H*-indolyl, isoquinolinyl, quinolinyl, or naphthyl ring;

(b) R^x is hydrogen or C_{1-4} aliphatic and R^y is T-R^3, or R^x and R^y are taken together with their intervening atoms to form an optionally substituted 5-7 membered unsaturated or partially unsaturated ring having 1-2 ring heteroatoms; and

(c) $R^{2'}$ is hydrogen or methyl and R^2 is T-W-R^6 or R, wherein W is $-C(R^6)_2O-$, $-C(R^6)_2N(R^6)-$, -CO-, $-CO_2-$, $-C(R^6)OC(O)-$, $-C(R^6)_2N(R^6)CO-$, $-C(R^6)_2N(R^6)C(O)O-$, or $-CON(R^6)-$, and R is an optionally substituted group selected from C_{1-6} aliphatic or phenyl, or R^2 and $R^{2'}$ are taken together with their intervening atoms to form a substituted or unsubstituted benzo, pyrido, pyrimido, or partially unsaturated 6-membered carbocyclo ring.

4. The compound according to claim 2, wherein said compound has one or more features selected from the group consisting of:

(a) Ring D is an optionally substituted ring selected from phenyl, pyridinyl, piperidinyl, piperazinyl, pyrrolidinyl, morpholinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, 2,3-dihydro-1*H*-isoindolyl, 2,3-dihydro-1*H*-indolyl, isoquinolinyl, quinolinyl, or naphthyl;

(b) R^x is hydrogen or methyl and R^y is -R, $N(R^4)_2$, or -OR, or R^x and R^y are taken together with their intervening atoms to form a 5-7 membered unsaturated or partially unsaturated ring having 1-2 ring nitrogens, wherein said ring is optionally substituted with -R, halo, oxo, -OR, $-C(=O)R$, $-CO_2R$, -COCOR, $-NO_2$, -CN, $-S(O)R$, $-SO_2R$, -SR, $-N(R^4)_2$, $-CON(R^4)_2$, $-SO_2N(R^4)_2$, $-OC(=O)R$, $-N(R^4)COR$, $-N(R^4)CO_2$(optionally substituted C_{1-6} aliphatic), $-N(R^4)N(R^4)_2$, $-C=NN(R^4)_2$, -C=N-OR, $-N(R^4)CON(R^4)_2$, $-N(R^4)SO_2N(R^4)_2$, $-N(R^4)SO_2R$, or $-OC(=O)N(R^4)_2$; and

(c) each R^5 is independently selected from halo, oxo, CN, NO_2, $-N(R^4)_2$, $-CO_2R$, $-CONH(R^4)$, $-N(R^4)COR$, $-SO_2N(R^4)_2$, $-N(R^4)SO_2R$, -SR, -OR, -C(O)R, or a substituted or unsubstituted group selected from 5-6 membered heterocyclyl, C_{6-10} aryl, or C_{1-6} aliphatic.

5. The compound according to claim 4, wherein:

(a) Ring D is an optionally substituted ring selected from phenyl, pyridinyl, piperidinyl, piperazinyl, pyrrolidinyl, morpholinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, 2,3-dihydro-1*H*-isoindolyl, 2,3-dihydro-1*H*-indolyl, isoquinolinyl, quinolinyl, or naphthyl;

(b) R^x is hydrogen or methyl and R^y is -R, $N(R^4)_2$, or -OR, or R^x and R^y are taken together with their

intervening atoms to form a 5-7 membered unsaturated or partially unsaturated ring having 1-2 ring nitrogens, wherein said ring is optionally substituted with -R, halo, oxo, -OR, -C(=O)R, -CO_2R, -COCOR, -NO_2, -CN, -S(O)R, -SO_2R, -SR, -$N(R^4)_2$, -$CON(R^4)_2$, -$SO_2N(R^4)_2$, -OC(=O)R, -$N(R^4)$COR, -$N(R^4)CO_2$(optionally substituted C_{1-6} aliphatic), -$N(R^4)N(R^4)_2$, -C=NN$(R^4)_2$, -C=N-OR, -$N(R^4)CON(R^4)_2$, -$N(R^4)SO_2N(R^4)_2$, -$N(R^4)SO_2$R, or -OC(=O)$N(R^4)_2$; and

(c) each R^5 is independently selected from halo, oxo, CN, NO_2, -$N(R^4)_2$, -CO_2R, -CONH(R^4), -$N(R^4)$COR, -$SO_2N(R^4)_2$, -$N(R^4)SO_2$R, -SR, -OR, -C(O)R, or a substituted or unsubstituted group selected from 5-6 membered heterocyclyl, C_{6-10} aryl, or C_{1-6} aliphatic.

6. The compound according to claim 4, wherein said compound has one or more features selected from the group consisting of:

(a) R^x and R^y are taken together with their intervening atoms to form a 6-membered unsaturated or partially unsaturated ring having 1-2 ring nitrogens, optionally substituted with halo, CN, oxo, C_{1-6} alkyl, C_{1-6} alkoxy, (C_{1-6} alkyl)carbonyl, (C_{1-6} alkyl)sulfonyl, mono- or dialkylamino, mono- or dialkylaminocarbonyl, mono- or dialkylaminocarbonyloxy, or 5-6 membered heteroaryl;

(b) each R^5 is independently selected from -halo, -CN, -oxo, -SR, -OR, -$N(R^4)_2$, -C(O)R, or a substituted or unsubstituted group selected from 5-6 membered heterocyclyl, C_{6-10} aryl, and C_{1-6} aliphatic; and

(c) $R^{2'}$ is hydrogen and R^2 is T-W-R^6 or R, wherein W is -$C(R^6)_2O$-, -$C(R^6)_2N(R^6)$-, -CO-, -CO_2-, -$C(R^6)$OC(O)-, -$C(R^6)_2N(R^6)$CO-, or -CON(R^6)-, and R is an optionally substituted group selected from C_{1-6} aliphatic or phenyl, or R^2 and $R^{2'}$ are taken together with their intervening atoms to form a substituted or unsubstituted

benzo, pyrido, or partially unsaturated 6-membered carbocyclo ring optionally substituted with -halo, oxo, $-N(R^4)_2$, $-C_{1-4}$ alkyl, $-C_{1-4}$ haloalkyl, $-NO_2$, $-O(C_{1-4}$ alkyl), $-CO_2(C_{1-4}$ alkyl), -CN, $-SO_2(C_{1-4}$ alkyl), $-SO_2NH_2$, $-OC(O)NH_2$, $-NH_2SO_2(C_{1-4}$ alkyl), $-NHC(O)(C_{1-4}$ alkyl), $-C(O)NH_2$, or $-CO(C_{1-4}$ alkyl), wherein the (C_{1-4} alkyl) is a straight, branched, or cyclic alkyl group.

7. The compound according to claim 6, wherein:

(a) R^X and R^Y are taken together with their intervening atoms to form a 6-membered unsaturated or partially unsaturated ring having 1-2 ring nitrogens, optionally substituted with halo, CN, oxo, C_{1-6} alkyl, C_{1-6} alkoxy, (C_{1-6} alkyl)carbonyl, (C_{1-6} alkyl)sulfonyl, mono- or dialkylamino, mono- or dialkylaminocarbonyl, mono- or dialkylaminocarbonyloxy, or 5-6 membered heteroaryl;

(b) each R^5 is independently selected from -halo, -CN, -oxo, -SR, -OR, $-N(R^4)_2$, -C(O)R, or a substituted or unsubstituted group selected from 5-6 membered heterocyclyl, C_{6-10} aryl, and C_{1-6} aliphatic; and

(c) $R^{2'}$ is hydrogen and R^2 is T-W-R^6 or R, wherein W is $-C(R^6)_2O-$, $-C(R^6)_2N(R^6)-$, -CO-, $-CO_2-$, $-C(R^6)OC(O)-$, $-C(R^6)_2N(R^6)CO-$, or $-CON(R^6)-$, and R is an optionally substituted group selected from C_{1-6} aliphatic or phenyl, or R^2 and $R^{2'}$ are taken together with their intervening atoms to form a substituted or unsubstituted benzo, pyrido, or partially unsaturated 6-membered carbocyclo ring optionally substituted with -halo, oxo, $-N(R^4)_2$, $-C_{1-4}$ alkyl, $-C_{1-4}$ haloalkyl, $-NO_2$, $-O(C_{1-4}$ alkyl), $-CO_2(C_{1-4}$ alkyl), -CN, $-SO_2(C_{1-4}$ alkyl), $-SO_2NH_2$, $-OC(O)NH_2$, $-NH_2SO_2(C_{1-4}$ alkyl), $-NHC(O)(C_{1-4}$ alkyl), $-C(O)NH_2$, or $-CO(C_{1-4}$ alkyl), wherein the (C_{1-4} alkyl) is a straight, branched, or cyclic alkyl group.

8. The compound according to claim 7, wherein said compound is selected from Table 3.

9. A composition comprising a compound according to any of claims 1-8 and a pharmaceutically acceptable carrier.

10. The composition according to claim 9 further comprising a second therapeutic agent.

11. A method of inhibiting GSK-3 or Aurora activity in a patient comprising the step of administering to a patient a therapeutically effective amount of the composition according to claim 9.

12. The method according to claim 11, wherein said method inhibits GSK-3 activity in a patient.

13. A method of inhibiting GSK-3 or Aurora activity in a biological sample comprising contacting said biological sample with the compound according to claim 1.

14. A method of treating a disease that is alleviated by treatment with an GSK-3 inhibitor, said method comprising the step of administering to a patient in need of such a treatment a therapeutically effective amount of the composition according to claim 9.

15. The method according to claim 14 further comprising the step of administering to a patient a second therapeutic agent.

16. The method according to claim 14, wherein said disease is diabetes.

17. The method according to claim 14, wherein said disease is Alzheimer's disease.

18. The method according to claim 14, wherein said disease is schizophrenia.

19. A method of enhancing glycogen synthesis in a patient in need thereof, which method comprises the step of administering to a patient a therapeutically effective amount of the composition according to claim 9.

20. A method of lowering blood levels of glucose in a patient in need thereof, which method comprises the step of administering to a patient a therapeutically effective amount of the composition according to claim 9.

21. A method of inhibiting the production of hyperphosphorylated Tau protein in a patient in need thereof, which method comprises the step of administering to a patient a therapeutically effective amount of the composition according to claim 9.

22. A method of inhibiting the phosphorylation of β-catenin in a patient in need thereof, which method comprises the step of administering to a patient a therapeutically effective amount of the composition according to claim 9.

23. A method of treating a disease that is alleviated by treatment with an aurora inhibitor, which method comprises the step of administering to a patient in need of such a treatment a therapeutically effective amount of the composition according to claim 9.

24. The method according to claim 23, further comprising the step of administering to a patient a second therapeutic agent.

25. The method according to claim 23 wherein said disease is cancer.